BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 50 (9), 2499—2500 (1977)

The Structure of Sendanolactone, a New Triterpenoid from *Melia azedarach* L. *var. japonica* Makino

Masamitsu Ochi, Hiyoshizo Kotsuki, Takashi Tokoroyama,* and Takashi Kubota**
Faculty of Science, Kochi University, Asakura, Kochi 780
**Faculty of Science, Osaka City University, Sugimoto-cho, Sumiyoshi-ku, Osaka 558*
***School of Medicine, Kinki University, Sayama-cho, Osaka 589*

(Received March 24, 1977)

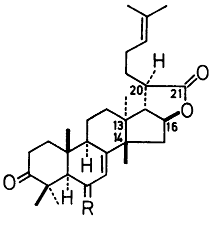
Synopsis. Sendanolactone, a new tetracyclic triterpenoid from the bark of *M. azedarach* L. *var. japonica* Makino, was determined as 3,6-dioxo-13α,14β,17α-lanosta-7,24-dien-21,16β-olide on the basis of chemical and spectroscopic evidence.

In the course of an investigation of limonoids of *M. azedarach* L. *var. japonica* Makino,1) a new tetracyclic triterpenoid was obtained. In this paper, the isolation and structural elucidation of this compound designated as sendanolactone is treated.

Sendanolactone (I), $C_{30}H_{42}O_4$, mp 208.5—209 °C, $[\alpha]_D^{14.5}$ −30° (*c* 0.1, EtOH), was isolated in a 0.008% yield from an methanol extract of the bark of *M. azedarach* L. *var. japonica* Makino by partitioning and careful silica gel column chromatography. The IR, UV, and NMR spectra of I indicate the presence of the following groups: one γ-lactone (1780 cm^{-1}), one six-membered ring ketone (1715 cm^{-1}), one α,β-unsaturated ketone [1655 and 1625 cm^{-1}; 246 nm (ε 16400)], five tertiary methyls [δ 1.00, 1.13, 1.34 (3H each, s), and 1.38 (6H, s)], two vinylic methyls [δ 1.64 and 1.72 (3H each, br s)], and one trisubstituted double bond [δ 5.11 (1H, m)]. The reduction of I with sodium borohydride in methanol, followed by acetylation, gave II, $C_{35}H_{52}O_7$, mp 204.5—205 °C, and III, $C_{36}H_{54}O_7$, mp 154.5—155 °C. The UV spectra of both products still showed the presence of the conjugated enones. The NMR spectrum of II indicates signals due to two acetate groups [δ 2.00 and 2.07 (3H each, s)] and a methyl ester [δ 3.62 (3H, s)], whereas that of III shows the presence of three acetate groups [δ 1.99, 2.04, and 2.07 (3H each, s)] and an acetylated hydroxymethyl [δ 4.03 (2H, d, *J*=4 Hz)], instead of the methyl ester. The formation of these products is explained as follows. The opening of the γ-lactone ring due to transesterification occurs concurrently with the reduction of the saturated ketone both in II and III during the sodium borohydride treatment, and further reduction of the resultant methoxycarbonyl group ensued in the latter.

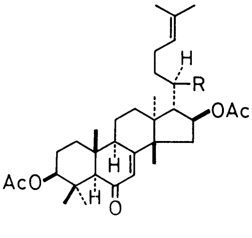
These facts and the analogy with the structures of the triterpenes isolated from the *Melia* species2) suggest a euphane or tirucallane skeleton for I, the side chain of which contains a double bond between C_{24} and C_{25}.

The location of the conjugated enones was proven by the following data. The NMDR experiments of I show the presence of a $-CO-CH_A{=}\overset{|}{C}-\overset{|}{C}H_B-$ grouping [δ_A 5.78 (1H, d, *J*=3 Hz) and δ_B 2.96 (1H, m)], in which the dihedral angle between H_A and H_B is roughly 90°. In the NMR spectrum of I, the signal due to the methine proton adjacent to the carbonyl appears as a sharp singlet (δ 2.46). Consequently, the conjugated enone must be located on the B-ring (7-en-6-one). Possible locations of γ-lactone are C_{21}–C_{23} and C_{21}–C_{16}. The NMR spectrum of I contains a signal due to the methine proton on an oxygenated carbon as a doublet of paired doublets (*J*=10, 10, and 8 Hz) at δ 4.18. This observation indicates that the oxy linkage of the lactone is at C_{16} and is β-oriented. From biogenetic considerations, it would be most reasonable to place the remaining carbonyl in I at C_3. This was verified by the following evidence. The NMR spectrum of I includes signals due to the methyls at C_4 and C_{10} at a rather low field [δ 1.38 (6H) and 1.33 (3H)], while those of II and III exhibit the corresponding signals at a somewhat higher field [II: δ 1.21 (6H) and 1.23 (3H); III: δ 1.19 (6H) and 1.21 (3H)]. Moreover, the solvent shifts ($\Delta=\delta^{CDCl_3}-\delta^{C_6D_6}$) of these signals in I, given in Table 1, are consistent with the case of 3,6-dione.3)



I R = O

IV R = H, H



II R = CO_2Me

III R = CH_2OAc

Table 1. Solvent shifts ($\Delta=\delta^{CDCl_3}-\delta^{C_6D_6}$) of C_4 and C_{10}-methyls in I

	δ^{CDCl_3}	$\delta^{C_6D_6}$	Δ
C_4-α-Me	1.38	1.64	−0.26
C_4-β-Me	1.38	1.42	−0.04
C_{10}-Me	1.33	0.82	+0.51

Therefore, sendanolactone must be represented by structure I.4) The proposed structure is quite analogous to that of kulactone (IV)2e) isolated from *M. azedarach* L., the typical variety, except for the presence of the ketonic group at C_6, and the spectral data of I are in good agreement with those of IV, except for the environment of the conjugated enone.

The structure of sendanolactone was eventually established from an X-ray analysis as 3,6-dioxo-13α,14β,17α-lanosta-7,24-dien-21,16β-olide (I),5) which is in full agreement with the structure derived from the chemical and spectral data mentioned above.

Sendanolactone is the first compound of the euphane series which has an oxygen substituent at C_6.

Experimental

All mps are uncorrected. The IR and UV spectra were recorded on a JASCO model IR-S and a Hitachi EPS-3T spectrophotometer, respectively. The NMR spectra were determined, using a JEOL PS-100 spectrometer, in $CDCl_3$ solutions with TMS as an internal standard unless otherwise stated. A Rex Optical Works model NEP-2 apparatus was used for the rotation measurement.

Isolation. Air-dried bark of *M. azedarach* L. *var. japonica* Makino (6 kg), collected in Kochi, in July 1974, was cut into small pieces and extracted with methanol (50 l) for one month. The methanol extract was concentrated up to about 5 l and washed with petroleum ether. The methanol layer was again concentrated up to 1 l, diluted with water (2 l), and extracted with ether. The ether layer was dried over Na_2SO_4 and evaporated to dryness. The residue (32 g) was repeatedly subjected to chromatography over silicic acid. Elution with $CHCl_3$–MeOH (49 : 1) gave sendanolactone (I) (470 mg): needles from methanol; mp 208.5—209 °C, $[\alpha]_D^{14.5}$ −30° (*c* 0.1, EtOH); MS *m*/*e* 466 (M^+). Found: C, 76.89; H, 9.12%. Calcd for $C_{30}H_{42}O_4$: C, 77.21; H, 9.07%.

Reduction of I With NaBH$_4$. To a solution of I (200 mg) in methanol (50 ml) were added excess amounts of $NaBH_4$ (200 mg). The mixture was stirred for 30 min at 0 °C. The solution was then concentrated, diluted with water (100 ml), and extracted with ether. The ether layer was washed with water, dried over Na_2SO_4, and evaporated to dryness. The residue was subjected to chromatography over silicic acid; subsequent elution with $CHCl_3$–MeOH (99 : 1) gave a diol and a triol.

The diol (84 mg) was acetylated with acetic anhydride (2 ml) and pyridine (2 ml) and then worked up in the usual manner to afford II (65 mg): needles from methanol, mp 204.5—205 °C; IR (Nujol) 1735 and 1660 cm^{-1}; UV (EtOH) 244 nm (ε 16700). Found: C, 71.93; H, 9.06%. Calcd for $C_{35}H_{52}O_7$: C, 71.88; H, 8.96%.

The triol (40 mg) was acetylated in the same manner as described above to give III (21 mg): needles from aqueous ethanol, mp 154.5—155 °C; IR (Nujol) 1740 and 1670 cm^{-1}; UV (EtOH) 245 nm (ε 12700). Found: C, 72.16; H, 9.06%. Calcd for $C_{36}H_{54}O_7$: C, 72.21; H, 9.09%.

We are grateful to Drs. M. Shiro and H. Nakai of Shionogi Research Laboratory for carring out the X-ray analysis and to Dr. Y. Hirose and Mr. H. Naoki of the Institute of Food Chemistry for recording the mass spectrum.

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4) The configuration at C_{20} is based on X-ray analysis. See also Ref. 5.

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